UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/713,860	11/17/2003	Constance Neely Wilson	5623-10	1884

826 7590 10/14/2008

ALSTON & BIRD LLP
BANK OF AMERICA PLAZA
101 SOUTH TRYON STREET, SUITE 4000
CHARLOTTE, NC 28280-4000

EXAMINER	
PARKIN, JEFFREY S	

ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
10/14/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/713,860	WILSON, CONSTANCE NEELY	
	Examiner	Art Unit	
	Jeffrey S. Parkin, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *03* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5,7,8,10,24,25 and 27-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-5,7,8,10,24,25 and 27-32* is/are rejected.

7)☒ Claim(s) *1* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *07/08/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Office Action

37 C.F.R. § 1.114

A request for continued examination under 37 C.F.R. § 1.114, including the fee set forth in 37 C.F.R. § 1.17(e), was filed in this application after final rejection on 08 July, 2008. Since this application is eligible for continued examination under 37 C.F.R. § 1.114, and the fee set forth in 37 C.F.R. § 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 C.F.R. § 1.114. Applicant's submission filed on 08 April, 2008, has been entered.

Status of the Claims

New claims 29-32 were introduced in the amendment filed 08 April, 2008. Claims 1, 3-5, 7, 8, 10, 24, 25, and 27-32 are pending in the instant application.

37 C.F.R. § 1.98

The information disclosure statement filed 08 July, 2008, has been placed in the application and the information referred to therein has been considered.

Claim Objections

Claim 1 is objected to because of the following informality: the term "adenosine deaminase deficiency-dependent severe immunodeficiency disease (ADA SCID)" should read --adenosine deaminase severe combined immunodeficiency disease (ADA-SCID)--. Appropriate correction is required.

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Claims 1, 3-5, 7, 8, 10, 24, 25, and 27-32 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claims 1, 3, 4, 10, 24, and 25 are directed toward a method of treating AIDS or ADA-SCID through the administration of an A_1 adenosine receptor antagonist, a P_{2X} purinoceptor antagonist, or a combination of both. Claims 5, 7, 8, 27, 28 are directed toward a method of preventing of delaying AIDS or ADA-SCID through the administration of an A_1 adenosine receptor antagonist, a P_{2X} purinoceptor antagonist, or a combination of both. Finally, claims 29-32 are directed toward a method of preventing or treating HIV infection through the administration of an A_1 adenosine receptor antagonist, a P_{2X} purinoceptor antagonist, or a combination of both.

The legal considerations that govern enablement determinations pertaining to undue experimentation have been

clearly set forth. *Enzo Biochem, Inc.*, 52 U.S.P.Q.2d 1129 (C.A.F.C. 1999). *In re Wands*, 8 U.S.P.Q.2d 1400 (C.A.F.C. 1988). *Ex parte Forman* 230 U.S.P.Q. 546 (PTO Bd. Pat. App. Int., 1986). The courts concluded that several factual inquiries should be considered when making such assessments including the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims. *In re Rainer*, 52 C.C.P.A. 1593, 347 F.2d 574, 146 U.S.P.Q. 218 (1965). The disclosure fails to provide adequate guidance pertaining to a number of these considerations as follows:

1) Adenosine deaminase severe combined immunodeficiency disease (ADA-SCID) results from a genetic defect in the ADA gene leading to multiple and complex organ problems (Hershfield, 2003). It is not readily manifest that simply providing a therapeutic agent would correct this deficiency since it fails to restore ADA activity and it fails to restore those tissues/organs that have been adversely affected by the deficiency. For instance, how would administration of an adenosine receptor antagonist or purinoceptor antagonist restore lymphocyte function? In the absence of a bone marrow transplant it is not clear how this administration would compensate for the underlying defect. To date, most therapeutic approaches have been directed toward restoring the enzymatic activity of this gene (Onodera *et al.*, 1999; Alessandro *et al.*, 2003; Javier *et al.*, 2004) and the depleted bone marrow population in an attempt to restore the immune system.

2) It is not readily manifest that A_1 adenosine receptor antagonists or P_{2x} purinoceptor antagonists would be efficient at inhibiting viral replication or reducing the viral burden associated with HIV infection. Nothing in the literature provides any nexus between HIV viral replication and A_1 adenosine receptor antagonist or P_{2x} purinoceptor antagonist administration. HIV is a difficult virus to treat because of the high number of virions generated per day and the ability of the virus to reside throughout the lymphatic compartment, often in a latent state (Ho *et al.*, 1995). Moreover, the administration of a non-specific therapeutic would also have deleterious effects on normal cellular and immune functions. The A_1 adenosine receptor and P_{2x} purinoceptor play a complex role in maintaining normal cellular function that is not limited solely to the immune system. Thus, inhibiting this normal pathway is likely to produce negative and undesirable effects as well.

3) The disclosure fails to provide any working embodiments demonstrating that ADA-SCID was effectively treated with A_1 adenosine receptor antagonists or P_{2x} purinoceptor antagonists. Considering the unpredictability associated with treating these disorders, several working examples would be required to enable the full breadth of the claimed invention. However, the disclosure is merely prophetic and fails to provide any data from an art-recognized animal model or preliminary clinical trials.

4) The disclosure fails to provide any working embodiments demonstrating that A_1 adenosine receptor antagonists or P_{2x} purinoceptor antagonists can reduce the viral burden associated with HIV infection and provide any meaningful clinical effect.

Considering the difficulty associated with treating HIV infection, several working examples would be required to enable the full breadth of the claimed invention. However, the disclosure is merely prophetic and fails to provide any data from an art-recognized animal model or preliminary clinical trials.

5) The state-of-the-art as it pertains to the treatment of ADA-SCID has been relatively unpredictable (Onodera *et al.*, 1999; Alessandro *et al.*, 2003; Javier *et al.*, 2004). Some gene therapy trials that restore ADA activity in conjunction with bone marrow transplants have shown promise, but once again, there is no data to suggest that A_1 adenosine receptor antagonists or P_{2x} purinoceptor antagonists would be effective at restoring ADA activity.

6) The state-of-the-art as it pertains to the generation of HIV antivirals can be characterized by unpredictability (Gait and Karn, 1995; D'Souza et al., 2000). HIV antivirals generally are targeted toward specific viral gene products and effectively inhibit the functions or activities of said gene products. However, there is nothing to suggest that A_1 adenosine receptor antagonists or P_{2x} purinoceptor antagonists would effectively inhibit viral replication. Moreover, the proposed therapeutics are not specific to virally infected cells. Thus, all cells bearing an A_1 adenosine receptor or P_{2x} purinoceptor would be affected by the administration of any given antagonist. Since this treatment regimen is non-specific, it is not readily manifest how it would be effective at combating HIV infection. A_1 adenosine receptor and P_{2x} purinoceptor stimulation is associated with several positive events such as angiogenesis promotion, attenuation of neuroinflammation and demyelination,

normal inflammatory events, and the elimination of intracelluular bacteria (Salmon *et al.*, 1993; Tsutsui *et al.*, 2004; Clark *et al.*, 2007; Sluyter *et al.*, 2001; Placido *et al.*, 2006). Administration of a non-specific antagonist would be expected to adversely impact these events as well.

When all the aforementioned factors are considered *in toto*, the skilled artisan would reasonably conclude that undue experimentation would be required to practice the claimed invention.

Response to Arguments

Applicant argues the claimed invention is predicated upon the discovery that LPS binds to, and activates, A_1 adenosine receptors, leading to activation of HIV-1. The Examiner does not dispute this finding. However, the claims are drawn toward methods of treating/preventing HIV-1 infection and ADA-SCID. Several caveats were raised that have not been addressed with any meaningful scientific data. It was additionally argued that A_1 adenosine receptors clearly play a role in ADA-SCID. The Examiner does not dispute this finding either. However, it still does not address the various flaws pointed out in the enablement rejection. Simply providing an A_1 adenosine receptor antagonist would not be expected to restore normal immune functions that have been depleted/destroyed by the deficiency. Applicant further argues that the nexus between LPS/HIV-1 expression/A_1 adenosine receptor stimulation demonstrates that his is a biologically relevant interaction. Once again, the Examiner does not dispute this finding. However, several HIV-1 antivirals have been ineffective for a number of reasons

previously set forth. Moreover, most HIV-1 antivirals are specific for the virus or virally infected cells. However, since numerous cell types express A_1 adenosine receptors and/oror P_{2x} purinoceptors, it seems reasonable that administering a compound that binds non-specifically to all these cell types would be less efficacious and potentially induce undesirable side-effects. No objective experimental data has been provided by Applicant to rebut this assertion. Additional arguments suggest that a working embodiment is not necessary. As set forth *supra*, considering the unpredictability of the field and the non-specific nature of the antagonists, multiple working embodiments would be required to enable the full breadth of the claimed invention. Finally, it was asserted that one of ordinary skill in the art could readily practice the claimed invention and that the previous difficulties encountered in the state-of-the-art were not relevant considering Applicant's disclosure. This argument is also persuasive for the reasons set forth in the preceding rejection. The development of antivirals, in particular, has been a difficult process. Moreover, the treatment of an immune deficiency wherein the underlying defect is enzymatic and results in organ destruction and dysfunction is unlikely to be effectively treated by simply administering a receptor antagonist.

Correspondence

Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (571) 272-0908. The examiner can normally be reached Monday through Thursday from 10:30 AM to 9:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Bruce R. Campell, Ph.D., can be reached at (571) 272-0974. Direct

general status inquiries to the Technology Center 1600 receptionist at (571) 272-1600. Informal communications may be submitted to the Examiner's RightFAX account at (571) 273-0908.

Applicants are reminded that the United States Patent and Trademark Office (Office) requires most patent related correspondence to be: a) faxed to the Central FAX number (571-273-8300) (updated as of July 15, 2005), b) hand carried or delivered to the Customer Service Window (now located at the Randolph Building, 401 Dulany Street, Alexandria, VA 22314), c) mailed to the mailing address set forth in 37 C.F.R. § 1.1 (e.g., P.O. Box 1450, Alexandria, VA 22313-1450), or d) transmitted to the Office using the Office's Electronic Filing System. This notice replaces all prior Office notices specifying a specific fax number or hand carry address for certain patent related correspondence. For further information refer to the Updated Notice of Centralized Delivery and Facsimile Transmission Policy for Patent Related Correspondence, and Exceptions Thereto, 1292 Off. Gaz. Pat. Office 186 (March 29, 2005).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,

/Jeffrey S. Parkin, Ph.D./
Primary Examiner, Art Unit 1648

30 September, 2008